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ORIGINAL ARTICLE

Incidence and outcome of critically ill patients with COVID-19 and Acute kidney Injury in tertiary care centre of north-west India

Shashank Bhardwaj*, Seetaram Singh*, Tushar Gupta*, Dhananjai Agrawal, Vinay Malhotra**, Rakesh Gupta***, Niranjan Gogoi*, Gigin SV*, Kavish Sharma*, Shivi******

ABSTRACT

Background: The clinical manifestations of the COVID-19 range from asymptomatic to a fulminant and rapidly fatal infection. Studies show that the incidence of acute kidney injury (AKI) in COVID-19 patients vary widely from 0.5 to 80%.

Objective:This study was conducted to study the incidence and outcome of critically ill patients having COVID-19 infection along with AKI at a tertiary care center.

Design:A prospective cohort study done over a period of one month.

Setting: In this study, all adult (⩾ 18 years) patients admitted in Intensive Care Unit (ICU) and have tested positive for COVID-19 via RT-PCR test were included. All patients found to have AKI were assessed for comorbidities like diabetes, hypertension, Coronary artery disease, Stroke etc. Patients were followed up during the hospital stay.

Results: Incidence of AKI among COVID-19 patients was found to be 32.3%. There was significant ($p<0.05$) association of incidence of AKI with cough, fever, high total leucocyte count, use of face mask, use of high flow mask, diabetes and coronary artery disease (CAD). Cough ($p=0.01$), use of face mask ($p=0.006$), invasive mechanical ventilation ($p=0.0001$) and hypertension ($p=0.03$) were significantly associated with mortality among these patients. Mortality was highest among patients of AKI stage III (95.7%).

Conclusion: Incidence of acute kidney injury in critically ill patients with COVID-19 hospitalized in a tertiary care centre in western part of India was high. AKI during hospitalization was associated with an increased risk of in-hospital death.

Keywords: COVID-19, Acute Kidney Injury, Critically ill

INTRODUCTION

In December 2019, a series of cases of acute respiratory illness occurred in Wuhan, Hubei Province, China. This disease was identified as COVID-19, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. On March 11, 2020, the World Health Organization announced that the COVID-19 virus was officially a pandemic after it spread to more than 114 countries in just 3 months. More than 16 months after the first reported case, the virus is still spreading at a rapid rate with more than 100 million affected and more than 3 million dead. As India is struggled with a devastating second wave, the health care resources have been stretched to the limit. Physician, including nephrologist have had to rapidly adapt their practice to handle the large number of cases presenting to them. The clinical manifestations of the Covid-19 range from asymptomatic to a fulminant and rapidly fatal infection. The primary target of coronavirus disease is, the lungs but high incidences of acute kidney injury (AKI) have been reported. Initially, an incidence of AKI in hospitalized COVID-19 patients has been reported to be 34%[1]. In critically ill patients the incidence increased to 78%[1]. But, further studies found that the incidence of AKI in COVID-19 patients to vary widely from 0.5% to 80%[2]. This study was conducted to describe the clinical characteristics and risk factors for AKI and death among critically ill patients of COVID-19 who were treated in the ICU of our hospital.

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MATERIALS AND METHODS

All patients presenting to the Intensive Care Unit (ICU) who tested positive for COVID-19 via RT-PCR were approached for inclusion into the study. Patient on immunosuppressive agents, with pre-existing chronic kidney disease and renal transplant recipients were excluded. After obtaining informed consent, a clinical profile was collected in a standard proforma. All patients found to have acute kidney injury were assessed for comorbidities like diabetes, hypertension, Coronary artery disease (CAD), stroke etc. Patients were followed up during the hospital stay and were assessed for need of oxygen (via face mask, high flow nasal cannula or high flow face mask), non-invasive or invasive mechanical ventilation. Proteinuria and hematuria were assessed using a dipstick. Need for vasopressors/ inotropes was assessed. Stage of AKI was calculated using KDIGO guidelines. Renal replacement therapy in the form of hemodialysis or peritoneal dialysis was used according to standard practice guidelines.

Definitions

AKI was identified according to the Guidelines of Kidney Disease: Improving Global Outcomes (KDIGO)[3]. It is defined as any of the following: an increase in Serum Creatinine of ⩾ 0.3 mg/dL within 48 hours; an increase in Serum Creatinine of ⩾ 1.5 times the baseline, which is known or presumed to have occurred within the past 7 days; or urine volume < 0.5 mL/kg/hr for 6 hours.

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ⩾0.3 mg/dl (⩾26.5 μmol/l) increase	<0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ⩾12 hours
3	3.0 times baseline OR Increase in serum creatinine to ⩾4.0 mg/dl (⩾353.6 μmol/l) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/h for ⩾24 hours OR Anuria for ⩾12 hours

RESULTS

The incidence of AKI was found to be 32.3%. Stage III AKI was among more than one third of patients (44.2%) followed by Stage I (28.8%) and Stage II (26.9%)Figure 1. About one third of patients were >60 years (34.2%). More than half of the patients were males (61.5%). The incidence of AKI was highest among patients of age >60 years (56.4%) and was lowest in <30 years (5%). The incidence of AKI was 24.54 times significantly higher among patients of age >60 years than <30 years (OR=24.54, 95%=3.06-196.50, p=0.003). The incidence of AKI was higher among males (36.4%) than females (25.8%), however, the association was statistically insignificant (p>0.05). Oxygen requirement was the most common (92.5%) and dyspnoea was the second most common factor (73.3%). CVA was the least common factor (5.6%). The incidence of AKI was 6.42 times significantly higher among whom dyspnoea was present than absent (OR=6.42, 95%CI=2.15-19.16, p=0.0001). There was significant (p<0.05) association of incidence of AKI with cough, fever, face mask, high flow mask, diabetes and CAD (Table 1). The incidence of AKI was 5.44 times significantly higher among whom TLC (Total Leukocyte Count) was abnormal than normal (OR=5.44, 95%CI= 2.00-14.82, p=0.0001). The factors found to be significant in univariate analysis were entered in the multivariate analysis. The multivariate analysis showed that the incidence of AKI was 12.44 times

significantly higher among patients of age >60 years than <30 years (Adjusted OR=12.44, 95%CI=1.42-127.76, p=0.03) when adjusted for dyspnoea and high flow mask. Dyspnoea (p=0.01) and high flow mask (p=0.0001) was also significantly associated with the incidence of AKI in multivariate model. Cough (p=0.01), face mask (p=0.006), invasive mechanical ventilation (p=0.0001) and hypertension (p=0.03) were significantly associated with mortality (Table 2). Mortality was higher among patients of AKI stage III (95.7%) than stage I (80%) and stage II (42.9%)Figure 2. The mortality was 82% significantly lower among patients of stage II than stage I (OR=0.18, 95%CI=0.03-0.97, p=0.04). Among the patients who developed AKI, we found the incidence of 1+, 2+, 3+ proteinuria to be 40%, 38% and 5.8% respectively. 15.4% of the patients had no proteinuria. Interestingly no patient in our study had 4+ proteinuria on dipstick examination. Concurrent haematuria of 1+ and 2+ was seen in 46.2% and 1.9% of the patients, respectively.

DISCUSSION

In this prospective cohort study conducted in Jaipur, Rajasthan, we observed an incidence of 32.3% of acute kidney injury in critically ill hospitalized patients with COVID-19. More than one third of these patients developed severe AKI, Stage III AKI. In our study, 14.28% of patients required renal replacement therapy.

The incidence of AKI reported in various studies varies from 0.5 to 80 percent[2]. In a meta-analysis[4] of approximately 13,000 mostly hospitalized patients, the incidence of AKI was 17 percent. Approximately 5 percent of patients required kidney replacement therapy (KRT) in this meta-analysis. The incidence of AKI seems to vary according to the number of critically ill patients included in the study. The high incidence of AKI in our study may be explained by the fact that we only included critically ill patients. The same may be the reason for higher number of patients requiring renal replacement therapy.

The incidence of AKI in critically ill patients, in pre COVID era has been found to be 39.3% in developed countries and 35.1% in the developing countries[5]. This is strikingly close to the incidence of AKI found in our study. The incidence of AKI was higher among the 2600 patients who had COVID-19 compared with over 19,500 patients who were hospitalized for other reasons (31 versus 18 percent)[6]. This higher incidence of AKI could not be explained by differences in the traditional risk factors for AKI between the groups. COVID-19 remained associated with a higher rate of AKI despite controlling for demographic variables, comorbidities, frequency of hypotension, selected laboratory results (eg, complete blood count, baseline eGFR), and use of nephrotoxic medications, vasopressors, or mechanical ventilation. Whether AKI in COVID-19 patients portents worse mortality outcomes than non-covid patients requires further study.

The etiology of AKI in critically ill patients with COVID-19 appears to be multifactorial. In AKI-EPI study done in pre-covid era, etiology of AKI in descending order was as follows: sepsis, hypovolemia, drug related, cardiogenic shock, hepatorenal syndrome, and obstructive uropathy[7].These are potential etiologies, even in critically ill patients of COVID-19 but whether SARS-CoV-2 causes a direct kidney infection remains controversial[8].The role of "cytokine storm" and the high incidence of thrombosis in patients of COVID-19 remain understudied causes of AKI in this Cohort[9,10].

A high incidence of AKI was seen in patients with respiratory failure. There was significant ($p<0.05$) association of incidence of AKI with oxygen requirement with a face mask or a high flow mask. Incidence of AKI was also higher among patients who required Non Invasive and Invasive mechanical ventilation, but the incidence was not found to be statistically significant.

In other studies, the incidence of AKI was higher in patients on high oxygen support[11].

Monitoring kidney function must therefore be emphasized even in patients with mild respiratory symptoms, and altered kidney function should be given particular attention after admission in clinical practice. Early detection and treatment of renal abnormalities, including adequate hemodynamic support and avoidance of nephrotoxic drugs, may help to improve the vital prognosis of COVID-19.

CT severity scores and markers of inflammation, such as C-reactive protein and ferritin, appeared to be

Table 1: Distribution of various factors and its association with incidence of AKI

Factors	No. (n=161)		With AKI		Without AKI		OR (95% CI)	P-value
	No.	%	No.	%	No.	%		
Dyspnea	118	73.3	48	40.3	70	59.7	6.42 (2.15-19.16)	0.0001*
Cough	72	44.7	15	20.8	57	79.2	0.37 (0.18-0.75)	0.005*
Fever	92	57.1	23	25	69	75	0.46 (0.23-0.90)	0.02*
Oxygen requirement	149	92.5	50	33.6	99	64.4	2.52 (0.53-11.96)	0.22
Nasal prongs	20	12.4	7	35.0	13	65.0	1.14 (0.42-3.07)	0.78
Face mask	28	17.4	1	3.6	27	96.4	0.06 (0.01-0.45)	0.0001*
High flow mask	22	13.7	14	63.6	8	36.4	4.65 (1.80-11.97)	0.001*
Non-invasive mechanical ventilation	52	32.3	18	34.6	34	65.4	1.16 (0.58-2.35)	0.66
Invasive mechanical ventilation	46	28.6	19	41.3	27	58.7	1.74 (0.85-3.56)	0.12
Diabetes	62	38.5	30	48.4	32	51.6	3.28 (1.65-6.52)	0.001*
Hypertension	63	39.1	26	41.3	37	58.7	1.94 (0.99-3.81)	0.06
CAD	17	10.6	10	58.8	7	41.2	3.46 (1.23-9.72)	0.01*
CVA	9	5.6	3	33.3	6	66.7	1.05 (0.25-4.37)	0.94
Need of vasopressors	48	29.8	19	39.6	29	60.4	1.58 (0.78-3.21)	0.19

OR-Odds ratio, CI-Confidence interval,*Significant

Table-2: Distribution of various factors and its association with mortality among critically ill patients.

Factors	No. of patients	Expired		Alive		OR (95%CI)	p-value
		No.	%	No.	%		
Dyspnea	118	61	51.7	57	48.3	1.63 (0.80-3.32)	0.17
Cough	72	27	37.5	45	62.5	0.44 (0.23-0.84)	0.01*
Fever	92	42	45.7	50	54.3	0.77 (0.41-1.43)	0.41
Oxygen requirement	149	73	49.0	76	51.0	1.34 (0.40-4.42)	0.62
Nasal Prongs	20	7	35.0	13	65.0	0.53 (0.20-1.40)	0.19
Face Mask	28	7	25.0	21	75.0	0.29 (0.11-0.73)	0.006*
High flow mask	22	10	45.5	12	54.5	0.87 (0.35-2.14)	0.76
Non-invasive Mechanical	52	21	40.4	31	59.6	0.61 (0.31-1.20)	0.15

Ventilation							
Invasive Mechanical Ventilation	46	38	82.6	8	17.4	8.90 (3.79-20.91)	0.0001*
Diabetes	62	36	58.1	26	41.9	1.87 (0.98-3.57)	0.06
Hypertension	63	37	58.7	26	41.3	1.97 (1.04-3.76)	0.03*
CAD (Coronary Artery Disease)	17	10	58.8	7	41.2	1.59 (0.57-4.42)	0.36
CVA (Cerebrovascular Accident)	9	5	55.6	4	44.4	1.35 (0.35-5.23)	0.66
Need for Vasopressors	48	25	52.1	23	47.9	1.23 (0.62-2.42)	0.54
Renal Replacement Therapy	23	21	91.3	2	8.7	14.92 (3.36-66.17)	0.0001*
Haemodialysis	11	9	81.8	2	18.2	5.28 (1.10-25.27)	0.02*
Peritoneal dialysis	14	13	92.9	1	7.1	16.40 (2.09-128.65)	0.001*
AKI	52	40	76.9	12	23.1	6.22 (2.92-13.26)	0.0001*

OR-Odds ratio, CI-Confidence interval, *Significant

higher among patients who had AKI compared with those who did not have AKI. However, the comparison between groups controlling for these inflammatory markers was not possible because the tests were not available for all the patients. A higher CT severity and marker of inflammation in those with AKI may be a pointer to a more severe disease, which may be the cause or effect or both in patients of COVID-19.

In our study, there was significant ($p<0.05$) association of incidence of AKI with older age, history of diabetes and CAD. There was a higher incidence of AKI among those with hypertension and history of CVA, but the incidence were not found to be statistically significant. Similarly, incidence of AKI was higher in those patients who required vasopressor support, but the incidence did not reach statistical significance. These are considered to be traditional risk factors for AKI. Patients with these comorbidities continue to be at risk for AKI, even among the patients of COVID-19 and frequent monitoring of renal functions of these patients may be warranted.

In our study, AKI was found to be significantly associated with mortality. Mortality was higher among patients of AKI stage III (95.7%) than stage I (80%) and stage II (42.9%). There was significant ($p<0.05$) association of mortality with requirement of renal replacement therapy. AKI has been found to be a risk factor for mortality in various studies of both COVID and non-COVID patients[11,12]. Whether AKI in COVID-19 patients portents worse mortality outcomes than non-COVID patients requires further study.

Among the patients who developed AKI, we found the incidence of 1+, 2+. 3+ proteinuria to be 40%, 38% and 5.8% respectively. 15.4 % of the patients had no proteinuria. Interestingly, no patient in our study had 4+ proteinuria on dipstick examination. Concurrent hematuria of 1+ and 2+ was seen in 46.2% and 1.9% respectively.

In most studies, where kidney biopsy was done in patients of COVID-19, the predominant kidney pathological finding was Acute Tubular Necrosis (ATN), but glomerular lesions have been reported in a minority of patients[13-17]. These findings explain the urinalysis findings in our patients. A renal biopsy could not be carried out in patients in our centre due to resource limitations, and the fact that all patients enrolled in the study were critically ill and many were haemodynamically unstable.

Even though this study included a substantial number of patients from a tertiary care hospital, it has several limitations. First, a baseline serum creatinine was not available for all patients, which may have led to an underestimation/overestimation of AKI or erroneous associations. Second, clinical data of patients after discharge were lacking, so we could not assess COVID-19 effects on long-term outcomes. The precise impact of COVID-19 on kidney structure and function and the incidence of chronic kidney disease in these patients require further investigation.

Our study represents the reality of public hospitals in our country. The findings described here, can help, not only in planning of future studies but also in

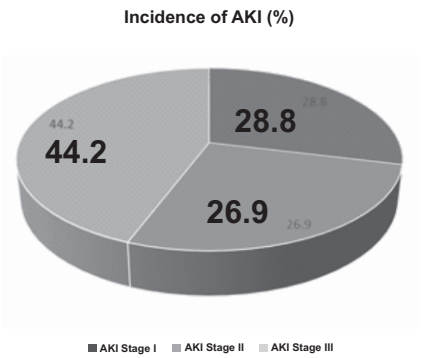

Figure 1: Incidence of AKI in COVID-19 patients according to AKI stages.

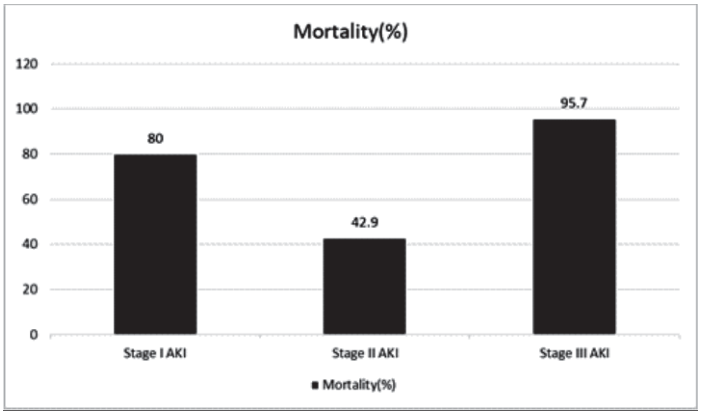

Figure 2: Mortality according to stages of AKI in COVID-19 patients

future planning of ICU care for critically ill patients of COVID-19. A high number of critically ill patients required renal replacement therapy and provisions for the same are an essential part of care for critically ill patients. The facility for the same is lacking in large parts of the country, and requires urgent attention.

In conclusion, the incidence of acute kidney injury in critically ill patients with COVID-19 hospitalized in Jaipur, was high. AKI during hospitalization was associated with an increased risk of in-hospital death. Clinicians should increase their awareness of kidney disease in hospitalized patients with COVID-19. Early detection and effective intervention of kidney involvement may help to reduce deaths of patients with COVID-19.

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REVIEW ARTICLE

Overview of Materiovigilance Programme of India

Arun Singh*, Monica Jain, Rupa Kapadia**, UmaAdvani***, Dhirendra Kumar Mahawar****, Shivankan Kakkar****, Jaya Dadhich *****

ABSTRACT

The Medical devices vigilance also known as Materiovigilance, is the collection,assessment, reporting and identification of trends in incidents resulting from the uses of medical devices (ex. instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article etc.). To ensure the safety of medical devices in India, a Materiovigilance Programme of India (MvPI) has been implemented from government of India in 2013 and it was formally launched on July 6, 2015, with collaboration of Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) as the National Coordinating Center (NCC). The collected and generated safety data will support to Central Drug Standard Control Organisation (CDSCO) for giving recommendation for safe use of medical devices in Indian population.

Keywords: Central Drug Standard Control Organisation (CDSCO), Materiovigilance, Medical Device, Safety.

INTRODUCTION

Materiovigilance is the supervision of adverse events occurring due to use of medical devices in patients. It is helping to develop the healthcare system of India. The word materiovigilance is derived from two Greek words “materio"- which means materials and "vigilare" meaning to keep awake or alert, to keep watch.Materiovigilance, as defined by the World Health Organization (WHO), is the science and activities relating to the detection, assessment, understanding and prevention of adverse events caused by medical devices. The purpose of medical devices for the identification, treatment, diagnosis, and cure of illness that may sometimes initiate adverse reactions which needs to be monitored and prevented. So, thus a vigilance system is required to supervise the adverse events[1]. In the beginning, the marketed medical devices were regulated according to the Drugs and Cosmetics Act, 1940 and Rules 1945. After that in year 2017, an absolute rule was outlined to regulate the medical devices that existing in the Indian market called as Medical Device Rules, 2017[2].

Medical device includes any instrument, implant, machine, appliances, equipment, grafting material, reagent for in vitro use or other article used on itself or combinedly as well as software needed for it to function properly, which is proposed to be used on patients by manufactures for the following scopes[3]:

(a) For diagnostic, prevention, control, treating or lessening the diseases.

(b) For diagnostic, control, treating, for reducing or counteracting an injury, impairment, and disabilities.

(c) For learning, substituting, or altering component of the anatomy or a physiological process.

(d) For grand achievement in conception.

MATERIOVIGILANCE PROGRAMME OF INDIA

In current scenario, there are need to regulate the safety surveillance of medical devices in India for prevention of unexpected events due to uses of medical device. The Ministry of Health and Family Welfare (MOHFW) has authorized the MvPI, an organisation for monitoring the safety of medical equipment affiliated from the Government of India in year 2013. The MvPI was officially introduced on July 6, 2015 at Indian

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Pharmacopoeia Commission (IPC), Ghaziabad by the Drugs Controller general India (DCGI). All prescriber, nursing officers and patients/consumers be made able to report Medical Devices Associated Adverse Events (MDAEs) to SreeChitraTirunal Institute of medical Sciences & technology (SCTIMST), Thiruvananthapuram or National Coordination Centre (NCC) - IPC[4]. The reported, collected and generated safety data will support to make easier in giving recommendations to Central Drugs Standard Control Organisation (CDSCO) and on directing of safe use of medical devices in Indian Population. Due to increasing number of cases of malfunctioning in many medical equipments and numerous medical device related adverse events, developing to further complications in patients and in most severe cases life-threatening conditions, the significance and necessity of MvPI are rising from previously days. Soon after in year 2018 onward, the IPC functions as NCC for MvPI as well NCC for Pharmacovigilance Programme in India (PvPI). MvPI has Medical Device Adverse Events Monitoring Centres (MDMCs) all over the country. To make sure effective of Adverse Events reporting from all respective individuals centres, this programme had established several tools for Adverse Event reporting to create India specific data[5]. For implementation of MvPI effectiveness, it is recognized that the integration of biomedical engineering department (BMED) at the health facilities/institutions is fundamental for further harmonisation with other departments. Hence, for functions as MDMCs, the preferences have been given to the institutes with BMED.

Different Medical Device Adverse Events Monitoring Centres Across India:

In India, there are ten MDMCs which have been recognized under MvPI that work to report MDAEswhose counts has been expanded to 150. Since 2015, the adverse events reporting rate has also increased. Through MvPI, more than 7000 reports have been submitted to IPC, Ghaziabad. For appropriate identification, reporting and collection of any suspected or definite MDAEs, MDMCs are responsible. MDAEs are classified into five categories: not related, unlikely, possible, probable, and causal relationship, respectively. MDMCs will send the reported data to NCC-IPC every month for review and analysis. IPC, Ghaziabad is the individual custodian of MvPI database. NCC is responsible to coordinate with all MDMCs nationwide and connects all concerned issues to the CDSCO. Apart from this, they collaborate with global authorities. It also provides financial support to SCTIMST, the National Health Systems Resource Centre (NHSRC), and MDMCs. SCTIMST functions as the NCC and gives help in all technical matters. NHSRC works as a technical support partner in the MvPI. Ultimately, all concerns are transferred to the CDSCO, i.e., a national regulatory authority ensuring safety. CDSCO is responsible for taking decisions on recommendations by the NCC-MvPI. The organizational structure of MvPI is represented in Figure 1.

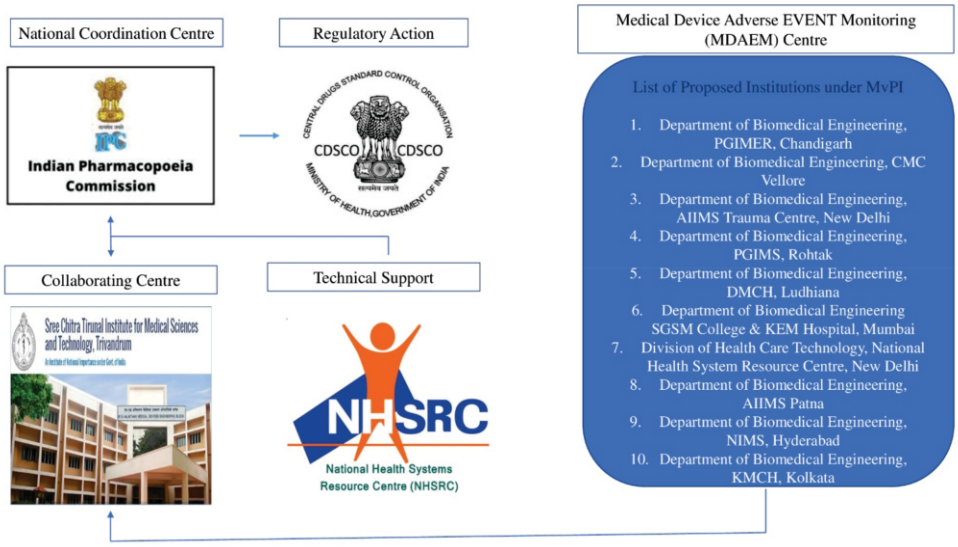

Figure 1: Diagrammatic Representation of MDEM Under MvPI

OBJECTIVES OF MATERIOVIGILANCE PROGRAM OF INDIA

The MvPI was began with the objectives to make safe the healthcare system and make sure the safety of medical device users and others by decreasing the recurrences of adverse events and malfunctions of medical eqipments[6].

The objectives are:

(a) To generate a countrywide system for monitoring of patient safety

(b) To scrutinise the risk–benefit ratio of medical equipment uses

(c) To create evidence-based data on the safety of medical equipment

(d) To support CDSCO in making precise decision process on the use of medical equipment

(e) To convey the safety information on the use of medical equipment among stakeholders to diminish the risk

(f) To develop as a national coordination center of excellence for materiovigilance activities

(g) To work together with other healthcare organizations and international body for the exchange of data information and its management

Regulation of Medical Devices Under Drug and Cosmetic Act:

In our country, at present days only notified medical devices are regulated as Drugs under the Drugs and Cosmetics Act 1940 and Rules made there under in 1945 that are given as following[7] : (A) Substances used for in vitro diagnosis and surgical dressings, surgical bandages, surgical staples, surgical sutures, ligatures, blood and blood component collection bag with or without anticoagulant covered under sub-clause (i); (B)Substances including mechanical contraceptives (condoms, intrauterine devices, tubal rings), disinfectants and insecticides notified under subclause (ii); and (C) Devices notified from time to time under subclause (iv), of clause (b) of section 3 of the Drugs and Cosmetics Act, 1940

POST MARKETING SURVEILLANCE APPROACHES IN WORLDWIDE

In 2011, a global organization with the designation of International Medical Device Regulators Forum (IMDF) was establishedwith the primary goal of accelerating the coordination of international medical devices regulation and to reinforce the foundation of Global Harmonization Task Forces (GHTF). Ten countries participated in IMDF management committee i.e., Australia, Brazil, Canada, China, European Union, Japan, Russia, Singapore, South Korea, and USA. All these countries have founded their individual surveillance systems for active and passive monitoring of MDAEs. The United State of America (USA) has founded a universal recognized system known as Food and Drug Administration (FDA) for the monitoring of food, medications, vaccines, and medical devices. In the same country, a mandatory and voluntary two schemes of medical device reporting have also been proposed[8], whereas United Kingdom (UK) has "Vigilance Reporting Scheme" as well the "Adverse Event Scheme" for the post-marketing surveillance of medical devices[9].The medical device manufacturers must take Vigilance Reporting Scheme and they should report adverse events within prescribed timeline. Although, it is voluntary for the healthcare professionals, hospital engineers and patients / consumers to take Adverse Event Scheme and report immediately. This scenario is different in Europe as all medical devices related issues are handed directly through National Competency Authority (NCA) from the manufacturer, while it is compulsory for general prescribers, doctors, and nurses to report the adverse event to manufacturer as well as NCA.The manufacturers are needed to submit a preliminary report of the serious medical device related adverse event within 2 calendar days. Later this, if the manufacturer realizes any relation between a medical device and life threatening or death or any health hazard, the appraisal is required to be reviewed within 10 days. Apart from this, very less serious or non-seriouscases can be reported within 30 calendar days[10]. In Japan country, medical devices are being regulated by the Pharmaceutical and Medical Device Agency that approaches come under certain rules and regulations which are required to be fulfilled for certification, quality assurance, and licensing including Japanese medical products[11]. In France, the medical device related adverse events are regulated by the “National Surveillance Commission" which is also known as the “Commission of Materiovigilance”. In Australia, the regulatory body, "Therapeutic Goods Administration” come under the Department of Health of the Australian Government that

regulates the medical device related adverse events[12]. Therapeutic Goods Administration keep data upto 5 years. In Canada, "Health Canada" Regulatory Authority regulates and ensure that all medical devices are safe and rationally used in both phases: pre- and post marketing surveillance and should be reported within 10 days after the manufacturer of a medical device becomes aware of an incident. In India, as already discussed that "Materiovigilance Programme of India" has been regulated the medical device related adverse events and reported to IPC within 15 calendar days of becoming aware of an eventand for non-serious events reporting to be done within 30 calendar days.

Pharmacovigilance Vs Materiovigilance

Materiovigilance is differ from Pharmacovigilance as given following:

	Pharmacovigilance	Materiovigilance
1.Definition	Pharmacovigilance is a system of monitoring Safety and Effectiveness of Drugs and other Pharmaceuticals.	Materiovigilance is a system of Monitoring Safety and Effectiveness of a Medical Device.
2. Programme Name in India	Pharmacovigilance Program of India	Materiovigilance Program of India
3. Launched Programme	In 2010	In 2015
4. Location of National Coordination Centre	Indian Pharmacopoeia Commission, Ghaziabad, previously in AIIMS, Delhi.	Indian Pharmacopoeia Commission Ghaziabad, SCTIMST and NHSRC.
5. Regulation	Finally, CDSCO will take necessary action against ADRs.	Finally, CDSCO will take necessary action against MDAEs.
6. Numbers of centres	At present, India have 395 adverse drug reaction monitoring centres in various medical colleges.	In India, currently medical device adverse events monitoring centresnumber has been increased to 150.

Reporting of Medical Device associated Adverse Events (MDAEs)

What to Report

All types of suspected Medical Device related Adverse Events (MDAEs) can be reported whether they are serious or non-serious, frequent, or rare regardless of an established causal relationship. A Medicaldevice can be any material, implant, incubator, instrument, apparatus, reagent, and any diagnostic tests, etc. Adverse Events description, Details of adverse event including description of device (deficiency or malfunction), clarification of threats associated with that device and the associated risk of patients with previous use can be provided in the MDAEs reporting form.

Who can Report

Practitioners, Biomedical Engineers, Clinical Engineers, Hospital Technology Managers, Pharmacists, Nurses, Technicians can report medical device adverse events.

Why to Report?

All associated medical device related adverse events should be reported in order to protect public health. Any unreported adverse events may lead to serious or death of patients.

Where to Report

The Healthcare workers (doctors, nurses, dentists, pharmacists), Manufactures and Patient/Consumers can report MDAEs to SCTIMST or NCC. Duly filled MDAEs Reporting Form can be send to SCTIMST or NCC- MvPI, Biomedical Technology Wing, Poojappura, Thiruvananthapuram, 695012, Kerala, India or Can directly email with scanned copy of the duly filled form to mvpi@sctimst.ac.in.

How to Report

MDAEs Medical Device Adverse Event Reporting Form [Figure 2] can be downloaded from the website of IPC (www.ipc.gov.in) to report adverse event associated with medical devices. MDAEs can also be reported via PvPI helpline number (1800 180 3024) on weekdays from 9:00 am to 5:30 pm.

MEDICAL DEVICE ADVERSE EVENT REPORTING FORM

Materiovigilance Programme of India

FOR MDMC/NCC USE ONLY

Type of report: Initial ☐ Follow-up ☐ | Report No. :

A. PATIENT DETAILS

1. Patient Hospital ID ----------
2. Sex: M ☐ F ☐
3. Age at time of Event or Date of Birth _____
4. Weight (Kg)_____

B. EVENT DETAILS

1. Event description-

Reason for the Event(Tick) a) Electrical ☐ b) Mechanical ☐ c) Electronic ☐ d) Biocompatibility ☐ e) Clinical application error ☐

2. Severity of the event (Yes ☐ No ☐) if yes please specify following

☐ Death (__/__/____) ☐ cause congenital-anomaly ☐ Life threatening ☐ Required intervention to prevent death or impairment of body function

☐ Hospitalization/Prolonged impairment/damage ☐ Disability ☐ Other (specify).....

3. Date of event -(dd/mm/yyyy)

4. Location of the event- OPD ☐ IPD ☐ Others (Please specify).....

5. Device category: (A) Therapeutic ☐ Diagnostics ☐ Both ☐ (B) Implantable device ☐ Non Implantable device ☐

(C). Single use device ☐ Reusable device ☐ Reuse of manufacture marked single use device ☐

6. Date-

Last preventive maintenance	Last calibration

7. Location of device after the incident:

Place of use ☐ Place of reporter ☐ Place of Manufacture/vendor ☐ With patient or end user ☐

8. Is device in use after incident Yes ☐ No ☐

9. (A) Is same model device available in organisation? Yes ☐ No ☐ If yes, Quantity.....

(B) Organization - Healthcare facility ☐ Manufacturer ☐

C. MEDICAL DEVICE(S) DETAIL

Name of Medical Device (1)	Manufacturer (2)	Brand Name (3)	Model No. (4)	Serial No. (5)	Batch No./ Lot No. (6)	Catalogue No. (for instruments only)	Date of installation/ implantation/ explantation (8)	List of Accessories (9)

10. Actions taken immediately after incident

11. A Whether other medical devices were being used at same time with above device for therapeutic of diagnostic service? If yes, please specify.....

11 B. Any history of adverse event(s) from device with same serial/model/catalogue number. If yes please specify.....

D.REGULATORY DETAILS			E. REPORTER DETAILS of MvPI CENTRE
Manufacturer name: Regulator in Country of origin: Regulatory status in origin country:	Entity legally representing the Manufacture: Country:	Notified Body name in: (i) Country of Manufacturing : (iii) In India:	Name and Professional Address:_____ Pin:_____ E-mail_____ Tel. No. (with STD code)_____ Designation:_____ Signature:_____ Date of this report___ dd/mm/yyyy
F. Causality Assessment Details	Completed ☐	In Progress ☐	Awaited ☐
Additional Information:			
Confidentiality: The patient's identity is held in strict confidence and protected to the fullest extent. Programme staff is not expected to and will not disclose the reporter's identity in response to a request from the public. **Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the adverse event.**			

National Collaborating centre-Materiovigilance Programme of India.

Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) under the Department of Science & Technology, Government of India. Biomedical Technology Wing, Poojappura, Thrivananthapuram 695012,Kerala. Phone: 91- 471 – 2340411, Fax: 91- 471 -2341814, Email: head-bmtw@sctimst.ac.in.

National Coordination Centre-Materiovigilance Programme of India.

Indian Pharmacopoeia Commission (IPC), Ministry of Health and Family Welfare, Government of India, Sector-23,Rajnagar, Ghaziabad-20002, Tel.:0120-2783400, 2783401, and 2783392, FAX: 0120-2783311, Email. ipclab@vsnl.net, pvpi.ipcindia@gmail.com

Technical support and Resource Centre- Materiovigilance Programme of India.

National Health System Resource Centre (NHSRC), NIHFW campus Baba Gangnath marg, Munirka, New Delhi-110067, Phones: 011 26108982 / 83 / 84 / 92 /93, Fax: 011-26108994 Email: nhsrc.india@gmail.com.

Where to report

- **Duly filled Medical Device Adverse Event Reporting Form can be send to Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), National Collaboration Centre-Materiovigilance Programme of India), Biomedical Technology Wing, Poojappura, Thrivananthapuram 695012,Kerala,India.**
- **Or Can directly email the duly filled form to mvpi@sctimst.ac.in.**
- **Call on Helpline no. 1800 180 3024 to report Adverse event.**

Event description Details of adverse event including description of device (deficiency or malfunction), clarification of hazards associated with device and the associated risk of patient, user or person any possible risk to patient associated with previous use.

Additional Information Other relevant information related to treatment should be provided.

Figure 2: Medical Device Adverse Reporting Form

Example for Materiovigilance:

The manufacturer has issued a batch of blood glucose test strips. According to instructions the patients use the strips. Because of wrong readings, wrong insulin dosage was taken by the patient which leads to hypoglycaemic shock and hospitalization.

Another example is the patients facing problems related to malfunction of cardiac pacemaker that leads to output failure or failure to capture or pacemaker-medicated tachycardia or runaway pacemaker etc. Because of these problems patients can suffer syncope and cardiac arrest.

Future Prospects of Materiovigilance Programme of India

If the MvPI has to be successful, the contribution at root level has to be accelerated. So, there is need to provide awareness among health-care workers and the general public about MvPI has to be strengthened. For increasing the awareness, we should know what exactly to report, that is potential barriers in reporting MDAEs. If they reported to regulatory authorities timely, it will help to those diseased patients that will be affected due to deficiency and malfunctions of using medical devices. Academic curricula MBBS, Postgraduate programs, nursing, dental and paramedical courses should be updated to includeMvPI, and the knowledge of reporting MDAEs. The number of materiovigilance centres are increasing continuously for implementation of MvPI. MvPIhas key role in prevention of medical device associated health hazard.

CONCLUSION

In a few past years, the medical device's uses are found to be frequently by doctors across all over world including India. In spite of that, there are not satisfactory tool to safe guard the patients from the undesired events. Materiovigilance Programme of India is a good initiative to make sure the safety of medical device. This programme will be also significantly reducing the risk associated to the use of medical devices by avoiding the repetition of aversive effects. Therefore, it is the moral responsibility for all healthcare professionals to report MDMEs to IPC, Ghaziabad through submission of reporting form so that CDSCO can give recommendations to prevent medical device related health hazards.

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DRUG UPDATE

Linzagolix

Monica Jain*, ShivankanKakkar, Yatendra Singh*****

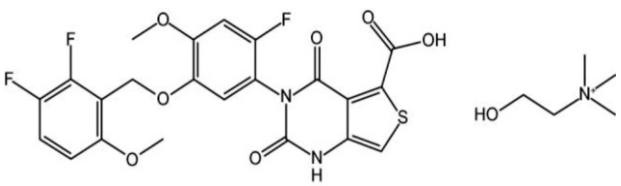
Linzagolix has been recently approved for the management of moderate-to-severe symptoms associated with leiomyomas (in the reproductive age group females) in the European Union (EU), whereas it is under regulatory review status in the United States of America (USA). Linzagolix is awaiting its entry in the Indian markets.

In the reproductive age group females, there are Oestrogen-related disorders like fibroids (uterine leiomyomas), endometriosis (endometrium-like tissue outside the uterine cavity) and adenomyosis (pathologically endometrial glands and stroma in uterine wall muscle).

Leiomyomas symptomatically present as- heavy menstrual bleeding (can result in anaemia), dysmenorrhea, pelvic pain, frequent urination, dyspareunia and it also increases risk for pregnancy complications, which are mainly managed surgically (mainly hysterectomy), Pharmacological management options available are like Gonadotropin releasing hormone (GnRH) agonists, Progestin-releasing IUD and Tranexamic acid. In recent studies, a promising alternative has emerged that is Linzagolix. It has been found to effectively improve symptoms with significant reduction in uterine volume.[1]

Chemical Name

3-{5-[(2,3-difluoro-6-methoxyphenyl)methoxyl]-2-fluoro-4-methoxyphenyl}-2,4-dioxo-1,2,3,4-tetrahydrothieno [3,4-d] pyrimidine-5-carboxylic acid



Linzagolix is a selective, non-peptide, orally active Gonadotropin releasing hormone (GnRH) antagonist, indicated for treatment of moderate-to-severe symptoms related with leiomyomas in reproductive age group females[2].

Preclinical data

In animal studies on ovariectomized cynomolgus monkey models reduction in serum LH levels at 8 hours was found which sustained for over 24 hours. Whereas, in intact female cynomolgus monkeys, dose -dependent partial or complete blockage of GnRHsignalling was seen, with resumption of normal menstrual cycles and hormonal secretion within one cycle on withdrawal[3].

Clinical trials data

In phase 1 trials, it was found that Linzagolix can be orally administered (taken with or without food) and gets rapidly absorbed. It is highly bound to plasma proteins, with a half-life of 15 hours. It is mainly excreted in urine, then in faeces, majorly unchanged[3].

Linzagolix in phase 2 and phase 3 trials effectively reduced pain and other symptoms and uterine and fibroid size as a selective GnRH receptor antagonist, blocking the hypothalamic pituitary-gonadal axis, resulting in dose dependent reduction in serum levels of luteinising hormone (LH), follicle-stimulating hormone (FSH) and estradiol. The GnRH receptors are coupled with Gaq/11 which on activation increases intracellular Ca^{2+} flux, Linzagolix dose-dependently inhibits GnRH-stimulated Ca^{2+} flux.

Linzagolix improved dysmenorrhea and non-menstrual pelvic pain in the randomised, double-blind, placebo-controlled phase 3 conducted in Europe and the USA in women with moderate-to-severe endometriosis-associated pain[3].

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Treatment with high-dose linzagolix 200 mg once daily for 12 weeks followed by a 100 mg/day maintenance dosage for a further 12 weeks significantly reduced uterine volume and adenomyosis-related symptoms, including pelvic pain and dysmenorrhea, in an exploratory phase 2 trial in 8 premenopausal women with symptomatic uterine adenomyosis[3] .

In clinical studies, the most common adverse events associated with Linzagolix were hot flushes and headache, more commonly at higher doses. These events were less frequent with Linzagolix with add-back therapy.

In phase 3 trials, less than 6 month use of Linzagolix 200 mg daily, reduction in size of leiomyomas was found, which may increase in size on cessation of drug. It should not be given more than 6 months due to risk of reduction of Bone Mineral Density on long term use[3].

In phase 3 trials, high lipid levels (LDL cholesterol, HDL cholesterol and triglycerides) were seen, which generally were higher in Linzagolix without add-back therapy (ABR). These levels reduced after the treatment but had not reached the baseline levels[3].

It should be given cautiously to patient with a history of depression and/or suicidal ideation as mood disorders like emotional lability, alteration in mood and depression are seen with use of GnRH antagonists including Linzagolix[3].

Relatively contraindicated for patients with moderate or severe kidney impairment or with end stage kidney disease and patients with severe hepatic impairment, as in these conditions unbound Linzagolix mean exposure is found increased[3].

Contraindicated in pregnancy or breastfeeding and patients with osteoporosis or genital bleeding of unknown aetiology.

Current status

Oral contraceptives and progestogens were effective in almost two-third females suffering from symptomatic leiomyomas. It is clinically known that oestrogen plays an important role in pathogenesis, oral GnRH antagonists may prove effective, especially in non-respondents to progestogens[4].

Linzagolix is approved for treatment of moderate-to-severe symptoms of leiomyomas in reproductive females in EU (17 June 2022) and in USA under regulatory review and under phase 3 clinical development for management of pain associated with endometriosis[3].

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CASE REPORT

A Rare Case of Pulmonary Nocardiosis in Late Post Renal Transplant Period

Tushar Gupta*, Vinay Malhotra, Seetaram Singh*, NiranjanGogoi*, Dhananjai Agrawal**, Gigin SV***

ABSTRACT

Nocardiosis is an uncommon but important infection in solid organ transplant recipients. It is a life-threatening disease in these patients. We report a case of 44- years-old kidney recipient who developed pulmonary nocardiosis that was successfully treated with intravenous imipenem and doxycycline in conjunction with a reduction in immunosuppressive therapy. This case emphasizes the role of new potent immunosuppressants and diabetes in the occurrence of opportunistic infections.In transplant recipients,who present with pulmonary symptoms and do not respond to usual antibiotics, a Nocardial infection should be suspected.

Keywords: Immunosuppressive therapy;Pulmonary nocardiosis; Renal transplantation.

INTRODUCTION

Nocardiosis is a lethal disease in solid organ transplant recipients. Nocardiosis belongs to the order Actinomycetales. It is a weakly acid fast, Gram-positive, branching filamentous aerobic bacteria. The most frequent species associated with infections in humans are Nocardia asteroids, Nocardiabra siliensis, Nocardia farscinica and Nocardia nova.

The usual mode of acquiring infection is through inhalation resulting in a pneumonitis followed by a dissemination of the infection, or can occur through skin trauma. It's three clinical forms include: cutaneous, pulmonary and disseminated. The cutaneous form is related to the transcutaneous inoculation and is common in tropical and warm temperate areas. The most common mode of transmission remains inhalation, resulting in pulmonary localization.

Nocardia is an opportunistic pathogen, causing pulmonary and systemic infections in immunocompromised patients. Patients in an immunocompromised state and having disseminated forms have poor prognosis.

In India, nocardiosis was reported in 1.4% of renal transplant recipients[1], most common species being Nocardia asteroids. Intense immunosuppression is the commonest predisposing factor.

We report herein a rare case of pulmonary nocardiosis developing in late post renal transplant period.

CASE REPORT

A 44 years old male patient, with end stage renal disease secondary to an unknown nephropathy, received renal transplantation in November 2019. The donor was his wife. They had 3 HLA mismatch. He had been treated for Hepatitis C before renal transplantation. He was given induction with Basiliximab and started on triple immunosuppressive therapy of Prednisolone, Tacrolimus and Mycophenolate mofetil. He had delayed graft function with serum creatinine being 4.1 mg/dl on postoperative day 7. Graft biopsy done, was reported as mixed rejection with acute tubular necrosis. He received methylprednisolone pulse therapy, intravenous immunoglobulin, plasmapheresis-4 sessions, 3 doses of anti-thymocyte globulin. Patient was discharged with good and stable renal function (serum creatinine of 1.5 mg/dl) on 15th postoperative day. New onset diabetes mellitus occurred fifteen months later and was managed by oral anti diabetic drugs.

In August 2021 (21 months post renal transplantation), he was admitted to the Nephrology department with complaints of fever, left sided pleuritic

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chest pain, shortness of breath along with cough and expectoration for 15 days.

Clinical examination revealed: body temperature of 39.6°C, respiratory rate of 28 per minute, blood pressure was 80/60 mm Hg, oxygen saturation of 82% on room air and 97% with 6 L/min oxygen support. Lung examination revealed tachypnoea and crepitations along left lung areas.

Laboratory investigations revealed haemoglobin of 14.8 m/dl, a total leucocyte count of 20,100/mm^3, neutrophils 90%, lymphocytes 6% and ESR was 58 mm in the first hour. Random blood sugar was 460 mg/dl. Renal function showed blood urea of 80 mg/dl and serum creatinine of 2.0 mg/dl. Other blood investigations which includes serum electrolytes and liver function tests were normal.

Chest radiograph showed non-homogenous opacity in left upper and lower zone [Figure 1]. CT chest revealed consolidation with internal air bronchogram, ground glass haziness in left upper and lower lobe suggestive of pneumonitis [Figure 2].

Microbiological investigations included sputum Gram stain which showed the presence of slender, Gram-positive, branching filamentous bacilli.

The patient was started on higher antibiotics, insulin infusion for blood sugar control and inotropic support for maintaining blood pressure. Sputum sent for modified Ziehl-Neelsen staining, revealed numerous acid-fast branching filamentous organisms, morphologically consistent with Nocardia species. [Figure 3].

Trimethoprim-sulfamethoxazole at therapeutic dose was added along with intravenous imipenem-based treatment and oraldoxycycline. Moreover, immunosuppressant drugs were temporarily reduced by decreasing dose of tacrolimus by 50% and stopping mycophenolate mofetil. Unfortunately, on treatment, the patient's condition got deteriorated and he succumbed to the illness.

DISCUSSION

Nocardiosis is aninfrequent infection and its diagnosis is difficult.Infection occurs in severely immunocompromised patient with reduced-cellular mediated immunitysuch solid organ transplants,human-immunodeficiency virus infected patients, auto-immunediseases, neoplasia and chronic lung disease.The most common risk factors are corticosteroid therapy and immunosuppression.

An observation by Carnet et al concluded that patients having Tacrolimus based immunosuppression were at increased risk for nocardiosis when compared to those on cyclosporin[2].

Our patient received induction treatment with Basiliximab and was maintained on mycophenolatemofetil, steroids, and Tacrolimus. He also received intravenous immunoglobulin, plasmapheresis, anti-thymocyte globulin for treatment of acute rejection. Moreover, diabetes mellitus is an additional risk factor favouring occurrence of opportunistic infection in our patient.

Nocardial infection is most common in first six months' post-transplant period[3]. Rarely reported after the first year of transplantation[4], but in our case presented after twenty-one month[5] post-transplant.

In pulmonary nocardiosis, the most common clinical presentationis a sub-acute or chronic necrotizing pneumonia. Pulmonary nocardiosis has a quintessential presentation, which includes fever, malaise, cough, anorexia, dyspnea, and chest pain. Our patient also had fever, cough and breathlessness as presenting complaints.

The most important diagnostic tool of pulmonary nocardiosis is Gram staining of sputum. However, no specific clinical or radiological features suggest nocardiosis. Only one third of sputum samples may show Nocardia, so multiple sputum specimens have to be examined.

Case studies showed that about 60-80% of nocardiosis in renal transplant patients is pulmonary nocardiosis and half of them have isolated lung involvement. A solitary pulmonary involvement was present in our patient without clinically apparent dissemination.

The most affected organs include: the lungs, skin, subcutaneous tissue and cerebro-nervous system. Other locations have been described: cardiac, ocular, osteoarticular.

So, for management of pulmonary nocardial infections, the key is to have a high index of suspicion, early diagnosis and adequate treatment. In transplant recipients, who present with pulmonary symptoms and do not respond to usual antibiotics, a Nocardial infection should be suspected.

Radiological patterns of pulmonary nocardiosis include, non-specific findings such as air space consolidation, presence of irregular nodular lesions, which may or may not associated with cavitation. Mediastinal and hilar lymphadenopathy may also be seen. In our patient, multilobar involvement was present with airspace consolidation but cavitation was lacking.

Prophylaxis with cotrimoxazole is recommended in renal transplant patients for pneumocystis carinï and urinary tract infection, and it is believed by some authors to protect from Nocardia infection. However, there is increasing cases of breakthrough infections in patients taking TMP-SMXprophylaxis.

Sulphonamides, mainly cotrimoxazole, are the treatment of choice, although other drugs, such as imipenem, amikacin, linelozid, cefotaxim, clarithromycin, ofloxacin, amoxicillin-clavulanic acid and tetracyc lines derivates are safe and effective.

Usually, six to nine months of antibiotic therapy, in case of localized pulmonary infections are needed and nine to twelve months in case of cerebro nervous system involvement.

Reduction of immunosuppression may be a helpful adjunctive therapy in severe forms of the disease but it is not a mandatory approach.

In pulmonary localization, mortality is about 40% and increases to 64% in disseminated nocardiosis and 100% in the presence of cerebro nervous system involvement5.

CONCLUSION

Transplant physicians should be aware of this rare infection and consider nocardiosis in differential diagnosis of pneumonia even in late post-transplant period, especially when the radiological features are atypicaland in patients who have not responded to the empirical treatment.

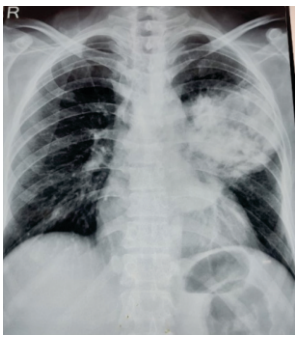

Figure 1. Chest X-ray

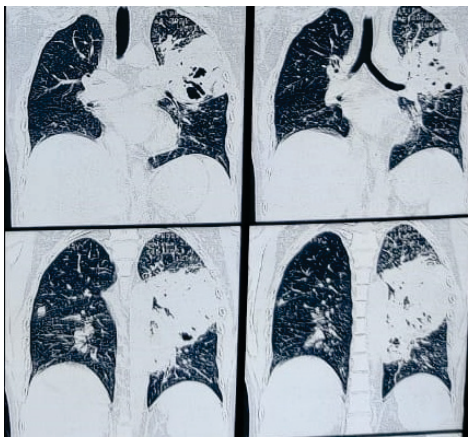

Figure 2. CT chest

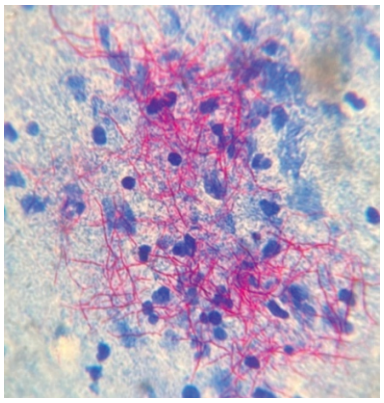

Figure 3. Modified ZiehlNeelsen stain

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KNOWLEDGE CORNER

Vaccination for Elderly: Easiest Way for Disease Prevention

Lakshmi Kant Goyal*, Sunny Singhal, Monica Jain***, Shashank Sharma******

The health problems faced by the elderly are unique compared to other age groups. In elderly, immune function are decreased predisposing this population prone for infectious diseases. The co-morbid conditions including chronic lung diseases and diabetes etc. make the infections more severe. The recovery from infections is also slow and usually takes longer time in elderly. In India, preventive care for diseases is often ignored among elderly (specially for age above 65 years). Many infections and illnesses could be easily avoided by administration of the right vaccines and diagnostic health screenings. Sadly, we don't have a National Immunization Schedule for the elderly as we have for children. It is expected from the family members to take proactive steps to vaccinate their older adults in the family to keep family stay healthy. Following is a brief note about preventive vaccination for older adults.

Elderly are more susceptible to the pneumococcal disease, influenza, herpes zoster, tetanus and COVID-19.

Pneumonia and other pneumococcal related diseases and their related complications are more common and severe in elderly compared to younger ones. For these people, pneumococcal vaccine is of two types: the 23-valent pneumococcal polysaccharide vaccine (PPSV23), and the 13-valent pneumococcal conjugate vaccine (PCV13). The PCV13 is more immunogenic. PPSV23 is less immunogenic but covers 10 more strains than PCV13. For our seniors, the recommended schedule is 1 dose PCV13 if previously did not receive PCV13, followed by 1 dose PPSV23 at least 1 year after PCV13. If previously received PPSV23 but not PCV13 at age 65 years or older; 1 dose PCV13 at least 1 year after PPSV23 is recommended. PCV13 and PPSV23 should not be administered during same visit. The recommended interval between PCV13 and PPSV23 is ≥1 year for immunocompetent elder. However, for those with immunocompromising or special conditions (chronic renal failure, nephrotic syndrome, blood cancer, generalized malignancy, solid organ transplant, multiple myeloma or splenectomy), the recommended time to wait is ≥8 weeks.

Influenza (flu) related morbidity and mortality is also higher in elderly. These people should receive 1 dose of inactivated influenza vaccine or a recombinant influenza vaccine annually preferably before the onset of influenza activity in the community, preferably in October before the flu season starts in India. Elderly should get a flu shot and not a nasal spray vaccine.

Herpes Zoster or Shingles, occurs when the chickenpox virus (dormant in almost all adults who had chickenpox in childhood); reactivates in later life. The condition often brings a blistering, painful rash. Post herpetic pain is more common and severe in elderly. There are 2 vaccines for shingles prevention. A live attenuated zoster vaccine (1-dose) and an adjuvant herpes zoster subunit vaccine (2 doses, administered 2 to 6 months apart, minimum 4 weeks interval). The adjuvanted herpes zoster subunit vaccine (2 dose vaccine) has higher efficacy. If the person had previously vaccinated with live attenuated zoster vaccine, then adjuvant herpes zoster subunit vaccine can be administered at least 2 months after. Live vaccines are contraindicated in severe immunocompromising conditions.

Diphtheria toxoid, tetanus toxoid and acellular pertussis-containing vaccines help in protecting against diphtheria, tetanus and pertussis, but they will not prevent

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all cases. Tdap (Tetanus and diphtheria toxoids and acellular pertussis vaccine), Td (Tetanus and diphtheria toxoids) and TT (Tetanus toxoid) are available. The elderly people should receive 1 dose Tdap, then Td or Tdap booster every 10 years. Previously TT was used as booster.

COVID-19 (CORONA) related pneumonia occurs in more severe form in elderly persons. Vaccination for COIVD-19 is also available and recommended for our seniors.

Apart from these vaccines for elderly, there are several other vaccines available i.e. Hepatitis B vaccine, which can be given according to the individual risk of getting infections.

Recommendation of vaccination in persons aged ≥ 65 years

Pneumococcal vaccine	Not previously vaccinated	A dose of PCV13 followed by a dose of PPSV23, 1 year after
	Previously vaccinated with only PPSV23	A dose of PCV13, one year after vaccination with PPSV23
	PPSV23 received at age < 65 years	PCV13 at age ≥ 65 years and PPSV23 after 1 year (at least 5 years after previous dose of PPSV23)
Influenza (flu)		Every year
Herpes Zoster	Adjuvant herpes zoster subunit vaccine (RZV)	2 doses, 2 to 6 months apart, minimum 4 weeks interval
	A live attenuated zoster vaccine (ZVL)	1 dose
Tetanus Toxoid	Tdap (Tetanus and diphtheria toxoids and acellular pertussis vaccine), Td (Tetanus and diphtheria toxoids)	1 dose Tdap, then Td or Tdap booster every 10 years
COVID-19 (CORONA) vaccine	Available	

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